

What is claimed:

1. A method of identifying RNA ligands which bind to a target molecule, said method comprising:
 - 5 treating a first pool of RNA ligands that collectively bind more than one target under conditions effective to reduce the concentration or eliminate the presence of one or more predominate target-binding RNA ligands from the first pool of RNA ligands;
amplifying the RNA ligands in the treated first pool, thereby
 - 10 forming a second pool of RNA ligands that is enriched in one or more non-predominate target-binding RNA ligands of the first pool but not the one or more predominate target-binding RNA ligands thereof; and
identifying from the second pool one or more predominate target-binding RNA ligands that are present in the second pool at a higher
 - 15 concentration than other target-binding RNA ligands.
2. The method according to claim 1 further comprising:
 - treating the second pool under conditions effective to reduce the concentration or eliminate the presence of one or more predominate target-binding
 - 20 RNA ligands;
amplifying the RNA ligands in the treated second pool, thereby forming a third pool of RNA ligands that is enriched in one or more non-predominate target-binding RNA ligands of the second pool but not the one or more predominate target-binding RNA ligands thereof; and
 - 25 identifying from the third pool one or more predominate target-binding RNA ligands that are present in the third pool at a higher concentration than other target-binding RNA ligands.
3. The method according to claim 2 wherein each said treating
- 30 comprises:
 - introducing into the pool to be treated one or more nucleic acid molecules that hybridize to the one or more predominate target-binding RNA ligands to form hybrid complexes and

introducing into the pool to be treated an enzyme which cleaves at least the RNA ligand of the hybrid complexes, thereby destroying the one or more predominate target-binding RNA ligands.

5 4. The method according to claim 1 further comprising repeating said treating, amplifying, and identifying for each subsequent pool until substantially all of the non-predominate target-binding RNA ligands in the first pool have been identified.

10 5. The method according to claim 4 wherein each said treating comprises:

 introducing into the pool to be treated one or more nucleic acid molecules that hybridize to the one or more predominate target-binding RNA ligands to form hybrid complexes and

15 introducing into the pool to be treated an enzyme which cleaves at least the RNA ligand of the hybrid complexes, thereby destroying the one or more predominate target-binding RNA ligands.

 6. The method according to claim 5 wherein the one or more
20 nucleic acid molecules are DNA and the enzyme is an RNaseH enzyme.

 7. The method according to claim 4 wherein each said identifying comprises:

 isolating the one or more predominate target-binding RNA

25 ligands and

 sequencing the one or more predominate target-binding RNA ligands.

8. The method according to claim 1 wherein said identifying comprises:
isolating the one or more predominate target-binding RNA ligands and
5 sequencing the one or more predominate target-binding RNA ligands.
9. The method according to claim 1 further comprising:
preparing the pool of RNA ligands that collectively bind to
10 more than one target and
identifying one or more predominate target-binding RNA ligands.
10. The method according to claim 9 wherein said preparing comprises:
15 expressing a library of RNA molecules that includes both RNA ligands that bind to at least one of one or more targets and RNA molecules that do not bind any of the one or more targets; and
partitioning the library of RNA molecules to form the first pool
20 of RNA ligands.
11. The method according to claim 10 wherein said expressing the library of RNA molecules comprises:
expressing a library of DNA molecules that includes both DNA
25 ligands that bind to at least one of one or more targets and DNA molecules that do not bind any of the one or more targets; and
transcribing the library of RNA molecules from the library of DNA molecules.
12. The method according to claim 1 wherein said treating comprises:
30 introducing into the first pool one or more nucleic acid molecules that hybridize to the one or more predominate target-binding RNA ligands to form hybrid complexes and

introducing into the first pool an enzyme which cleaves at least the RNA ligand of the hybrid complexes, thereby destroying the one or more predominate target-binding RNA ligands.

5 13. The method according to claim 12 wherein the one or more nucleic acid molecules are DNA and the enzyme is an RNaseH enzyme.

 14. The method according to claim 1 wherein the targets comprise natural or synthetic small molecules, macromolecules, supramolecular assemblies,
10 and combinations thereof.

 15. A method of reducing the concentration or eliminating the presence of unwanted target-binding species from a pool of RNA ligands, said method comprising:
15 providing a pool of RNA ligands which includes both wanted and unwanted target-binding RNA ligands;
 identifying one or more unwanted target-binding RNA ligands;
 and
 treating the pool under conditions effective to reduce the
20 concentration or eliminate the presence of the one or more unwanted target-binding RNA ligands from the pool of RNA ligands.

 16. The method according to claim 15 wherein said identifying comprises:
25 isolating the one or more unwanted target-binding RNA ligands
 and
 sequencing the one or more unwanted target-binding RNA
ligands.

17. The method according to claim 15 wherein said treating comprises:

introducing into the pool one or more nucleic acid molecules that hybridize to the one or more unwanted target-binding RNA ligands to form

5 hybrid complexes and

introducing into the pool an enzyme which cleaves at least the RNA ligands of the hybrid complexes, thereby destroying the one or more unwanted target-binding RNA ligands.

10 18. The method according to claim 17 wherein the one or more nucleic acid molecules are DNA and the enzyme is an RNaseH enzyme.

19. The method according to claim 17 wherein the one or more unwanted target-binding RNA ligands comprise one or more RNA ligands that bind to
15 a matrix used to partition the pool of RNA ligands from a library of RNA molecules.

20. The method according to claim 15 wherein the unwanted target-binding RNA ligands are RNA ligands that bind to a matrix, and wherein said treating comprises:

20 introducing into the pool one or more nucleic acid molecules that hybridize to the RNA ligands that bind to a matrix, thereby forming hybrid complexes and

introducing into the pool an enzyme which cleaves at least the RNA ligands of the hybrid complexes, thereby destroying the RNA ligands that bind
25 to a matrix.

21. The method according to claim 20 wherein the one or more nucleic acid molecules are DNA and the enzyme is an RNaseH enzyme.

30 22. The method according to claim 20 wherein the matrix is a nitrocellulose matrix.

23. An oligoDNA molecule that hybridizes to an RNA ligand, which binds to a partitioning matrix, and is capable of directing an RNaseH enzyme to cleave the RNA ligand in a hybrid complex formed by the oligoDNA molecule and the RNA ligand.

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24. The oligoDNA molecule according to claim 23 wherein the partitioning matrix is a nitrocellulose matrix.

25. The oligoDNA molecule according to claim 24 wherein the isolated oligoDNA molecule comprises a nucleotide sequence of any of SEQ ID Nos: 5-14, or combinations thereof.

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26. The oligoDNA molecule according to claim 23 in isolated form.

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27. A duplex formed between an oligoDNA molecule according to claim 23 and an RNA ligand that binds to a partitioning matrix.

28. The duplex according to claim 27 wherein the partitioning matrix is nitrocellulose.

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29. A kit for selecting RNA ligands that bind to one or more target molecules, said kit comprising:

a matrix for partitioning RNA ligands that bind to at least one of one or more target molecules from RNA ligands that do not bind to any of the one or more target molecules;

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the oligoDNA molecule according to claim 23; and
an RNaseH enzyme.

30. The kit according to claim 29 further comprising reagents for amplifying RNA ligands.

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31. The kit according to claim 29 wherein the oligoDNA molecule comprises a nucleotide sequence of any of SEQ ID Nos: 5-14.

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32. The kit according to claim 29 wherein the oligoDNA molecule comprises two or more oligoDNA molecules each comprising a nucleotide sequence of any of SEQ ID Nos: 5-14.

5 33. An nucleic acid aptamer that binds to a heat shock factor protein.

34. The nucleic acid aptamer according to claim 33 wherein the heat shock factor is a *Drosophila* heat shock factor.

10 35. The nucleic acid aptamer according to claim 33 wherein the nucleic acid aptamer comprises a nucleotide sequence according to SEQ ID NO: 31, 32, or 33.

15 36. The RNA aptamer according to claim 33 wherein the nucleic acid aptamer comprises a nucleotide sequence according to SEQ ID NO: 34, 35, or 36.

20 37. The nucleic acid aptamer according to claim 33 wherein the nucleic acid is RNA.

38. A multivalent RNA aptamer comprising two or more aptamers according to claim 37.

25 39. A method of modifying activity of a heat shock factor protein comprising:

binding the nucleic acid aptamer according to claim 33 to a heat shock factor protein under conditions effective to modify the activity of the heat shock factor protein.

30 40. The method according to claim 39 wherein the heat shock factor protein is a *Drosophila* heat shock factor protein.

41. The method according to claim 39 wherein the nucleic acid aptamer comprises a nucleotide sequence according to SEQ ID NO: 31, 32, or 33.

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42. The method according to claim 39 wherein the nucleic acid aptamer comprises a nucleotide sequence according to SEQ ID NO: 34, 35, or 36.

5 43. A method of modifying a stress response mediated by a heat shock factor protein comprising:

binding the nucleic acid aptamer according to claim 33 to a heat shock factor protein under conditions effective to modify the activity of the heat shock factor protein, thereby modifying a stress response mediated by the heat shock factor protein.

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44. The method according to claim 43 wherein the heat shock factor protein is a *Drosophila* heat shock factor protein.

15 45. The method according to claim 43 wherein the nucleic acid aptamer comprises a nucleotide sequence according to SEQ ID NO: 31, 32, or 33.

46. The method according to claim 43 wherein the nucleic acid aptamer comprises a nucleotide sequence according to SEQ ID NO: 34, 35, or 36.